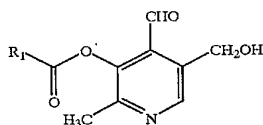


**CLAIMS****-43-**

What is claimed is:

1. A pharmaceutical composition comprising: (a) a HMG CoA reductase inhibitor; (b) a vitamin B6 related compound; and (c) a pharmaceutically acceptable carrier.
2. The pharmaceutical composition according to claim 1 wherein the HMG CoA reductase inhibitor is selected from a group consisting: pravastatin, lovastatin, fluvastatin, atorvastatin, simvastatin, rosuvastatin, velostatin, fluindostatin, and a mixture thereof.
3. The pharmaceutical composition according to claim 1 wherein the vitamin B6 related compound is selected from a group consisting: pyridoxal, pyridoxal-5'-phosphate, pyridoxamine, a 3-acylated analogue of pyridoxal, a 3-acylated analogue of pyridoxal-4,5-aminal, a pyridoxine phosphate analogue, and a mixture thereof.
4. The pharmaceutical composition according to claim 1 wherein the vitamin B6 related compound is pyridoxal-5-phosphate.
5. The pharmaceutical composition according to claim 3 wherein the 3-acylated analogue of pyridoxal is:



wherein,

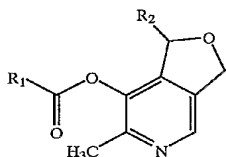
R<sub>1</sub> is alkyl, alkenyl, in which alkyl can be interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

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R<sub>1</sub> is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R<sub>1</sub> is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

6. The pharmaceutical composition according to claim 3 wherein the 3-acetylated analogue of pyridoxal-4,5-aminal is



wherein,

R<sub>1</sub> is alkyl, alkenyl, in which alkyl can be interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

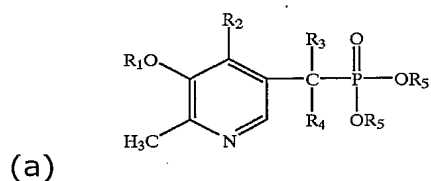
R<sub>1</sub> is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R<sub>1</sub> is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

R<sub>2</sub> is a secondary amino group.

7. The pharmaceutical composition according to claim 3 wherein the pyridoxine phosphate analogue is selected from a group consisting:

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wherein,

$R_1$  is hydrogen or alkyl;

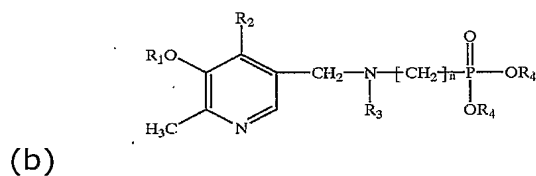
$R_2$  is  $-\text{CHO}-$ ,  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_3$ ,  $-\text{CO}_2\text{R}_6$  in which  $\text{R}_6$  is hydrogen, alkyl, aryl; or

$R_2$  is  $-\text{CH}_2-\text{O}$  alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of  $\text{R}_1$ ;

$\text{R}_3$  is hydrogen and  $\text{R}_4$  is hydroxy, halo, alkoxy, alkanoyloxy, alkylamino, or arylamino; or

$\text{R}_3$  and  $\text{R}_4$  are halo; and

$\text{R}_5$  is hydrogen, alkyl, aryl, aralkyl, or  $-\text{CO}_2\text{R}_7$  in which  $\text{R}_7$  is hydrogen, alkyl, aryl, or aralkyl;



wherein,

$\text{R}_1$  is hydrogen or alkyl;

$\text{R}_2$  is  $-\text{CHO}$ ,  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_3$ ,  $-\text{CO}_2\text{R}_5$  in which  $\text{R}_5$  is hydrogen, alkyl, aryl; or

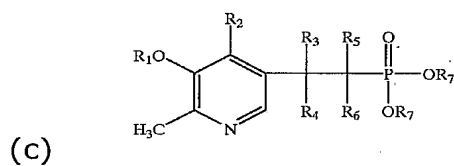
- 46 -

$R_2$  is  $-\text{CH}_2\text{-O}$  alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of  $R_1$ ;

$R_3$  is hydrogen, alkyl, aryl, aralkyl,

$R_4$  is hydrogen, alkyl, aryl, aralkyl, or  $-\text{CO}_2R_6$  in which  $R_6$  is hydrogen, alkyl, aryl or aralkyl;

$n$  is 1 to 6; and



wherein,

$R_1$  is hydrogen or alkyl;

$R_2$  is  $-\text{CHO}-$ ,  $\text{CH}_2\text{OH}-$ ,  $-\text{CH}_3$ ,  $-\text{CO}_2R_8$  in which  $R_8$  is hydrogen, alkyl, aryl; or

$R_2$  is  $-\text{CH}_2\text{-O}$  alkyl- in which alkyl is covalently bonded to the oxygen at the 3-position instead of  $R_1$ ;

$R_3$  is hydrogen and  $R_4$  is hydroxy, halo, alkoxy, or alkanoyloxy; or

$R_3$  and  $R_4$  can be taken together to form  $=\text{O}$ ;

$R_5$  and  $R_6$  are hydrogen; or

$R_5$  and  $R_6$  are halo;

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R<sub>7</sub> is hydrogen, alkyl, aryl, aralkyl, or -CO<sub>2</sub>R<sub>8</sub> in which R<sub>8</sub> is hydrogen, alkyl, aryl, or aralkyl.

8. A method for treating a patient at risk of cardiovascular disease comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 7.

9. The method according to claim 8, wherein the patient is susceptible to hepatotoxicity.

10. The method according to claim 8 wherein the cardiovascular disease is selected from a group consisting: congestive heart failure, myocardial ischemia, arrhythmia, myocardial infarction, ischemic stroke, hemorrhagic stroke, coronary artery disease, hypertension (high blood pressure), atherosclerosis (clogging of the arteries), aneurysm, peripheral artery disease (PAD), thrombophlebitis (vein inflammation), diseases of the heart lining, diseases of the heart muscle, carditis, congestive heart failure, endocarditis, ischemic heart disease, valvular heart disease (malfunction of a valve or valves in the blood vessels of the heart), arteriosclerosis (hardening of the arteries), acute coronary syndrome (ACS), deep vein thrombosis (DVT), Kawazaki disease, high cholesterol, restinosis, late vein graft failure and heart transplant.

11. The method according to claim 8 wherein the dose of the HMG CoA reductase inhibitor is between 0.1 and 1000 mg per day.

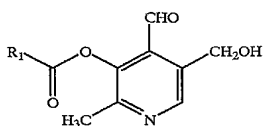
12. The method according to claim 8 wherein the dose of the HMG CoA reductase inhibitor is 10 mg per day.

13. The method according to claim 8 wherein the dose of the HMG CoA reductase inhibitor is 20 mg per day.

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14. The method according to claim 8 wherein the dose of the vitamin B6 related compound is between 0.1 to 50 mg/kg per day.
15. The method according to claim 8 wherein the dose of vitamin B6 related compound is between 1 to 15 mg/kg per day.
16. A method of a patient at risk for diabetes comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 8.
17. A method for treating a patient at risk of Alzheimer's disease comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 7.
18. A method for treating a patient at risk of osteoporosis comprising administering a therapeutically effective dose of the pharmaceutical composition according to any one of claims 1 to 7.
19. A method of treating or preventing hypercholesterolemia in a patient, comprising administering a therapeutically effective dose of a vitamin B6 related compound wherein the vitamin B6 related compound is selected from a group consisting: pyridoxal-5'-phosphate, a 3-acylated analogue of pyridoxal, a 3-acylated analogue of pyridoxal-4,5-aminal, a pyridoxine phosphate analogue, and a mixture thereof.
20. The method according to claim 19 wherein the vitamin B6 related compound is pyridoxal-5-phosphate.
21. The method according to claim 19 wherein the 3-acylated analogue of pyridoxal is:

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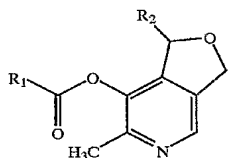
wherein,

R<sub>1</sub> is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R<sub>1</sub> is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

R<sub>1</sub> is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

22. The method according to claim 16 or 17 wherein the 3-acylated analogue of pyridoxal-4,5-aminal is



wherein,

R<sub>1</sub> is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

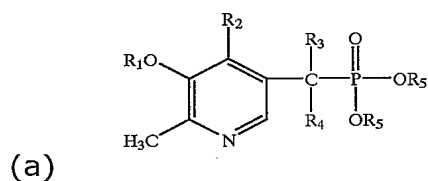
R<sub>1</sub> is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoyloxy; or

- 50 -

R<sub>1</sub> is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

R<sub>2</sub> is a secondary amino group.

23. The pharmaceutical composition according to claim 16 wherein the pyridoxine phosphate analogue is selected from a group consisting:



wherein,

R<sub>1</sub> is hydrogen or alkyl;

R<sub>2</sub> is -CHO-, -CH<sub>2</sub>OH, -CH<sub>3</sub>, -CO<sub>2</sub>R<sub>6</sub> in which R<sub>6</sub> is hydrogen, alkyl, aryl; or

R<sub>2</sub> is -CH<sub>2</sub>-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R<sub>1</sub>;

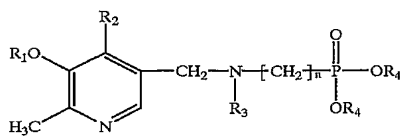
R<sub>3</sub> is hydrogen and R<sub>4</sub> is hydroxy, halo, alkoxy, alkanoyloxy, alkylamino, or arylamino; or

R<sub>3</sub> and R<sub>4</sub> are halo; and

R<sub>5</sub> is hydrogen, alkyl, aryl, aralkyl, or -CO<sub>2</sub>R<sub>7</sub> in which R<sub>7</sub> is hydrogen, alkyl, aryl, or aralkyl;



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(b)

wherein,

$R_1$  is hydrogen or alkyl;

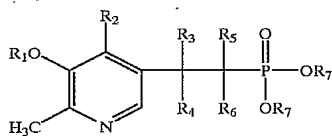
$R_2$  is  $-\text{CHO}$ ,  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_3$ ,  $-\text{CO}_2\text{R}_5$  in which  $\text{R}_5$  is hydrogen, alkyl, aryl; or

$R_2$  is  $-\text{CH}_2\text{-O}$  alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of  $\text{R}_1$ ;

$\text{R}_3$  is hydrogen, alkyl, aryl, aralkyl,

$\text{R}_4$  is hydrogen, alkyl, aryl, aralkyl, or  $-\text{CO}_2\text{R}_6$  in which  $\text{R}_6$  is hydrogen, alkyl, aryl or aralkyl;

$n$  is 1 to 6; and



(c)

wherein,

$\text{R}_1$  is hydrogen or alkyl;

$\text{R}_2$  is  $-\text{CHO}$ -,  $\text{CH}_2\text{OH}$ -,  $-\text{CH}_3$ ,  $-\text{CO}_2\text{R}_8$  in which  $\text{R}_8$  is hydrogen, alkyl, aryl; or

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R<sub>2</sub> is -CH<sub>2</sub>-O alkyl- in which alkyl is covalently bonded to the oxygen at the 3-position instead of R<sub>1</sub>;

R<sub>3</sub> is hydrogen and R<sub>4</sub> is hydroxy, halo, alkoxy, or alkanoyloxy; or

R<sub>3</sub> and R<sub>4</sub> can be taken together to form =O;

R<sub>5</sub> and R<sub>6</sub> are hydrogen; or

R<sub>5</sub> and R<sub>6</sub> are halo;

R<sub>7</sub> is hydrogen, alkyl, aryl, aralkyl, or -CO<sub>2</sub>R<sub>8</sub> in which R<sub>8</sub> is hydrogen, alkyl, aryl, or aralkyl.

24. A method for treating a patient at risk of cardiovascular disease, said patient being administered a HMG CoA reductase inhibitor, comprising administering a therapeutically effective dose of a vitamin B6 related compound and a pharmaceutically acceptable carrier.

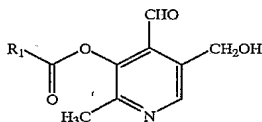
25. The method according to claim 24 wherein the HMG CoA reductase inhibitor is selected from a group consisting: pravastatin, lovastatin, fluvastatin, atorvastatin, simvastatin, rosuvastatin, velostatin, fluindostatin, and a mixture thereof.

26. The method according to claim 24 wherein the vitamin B6 related compound is selected from a group consisting: pyridoxal, pyridoxal-5'-phosphate, pyridoxamine, a 3-acylated analogue of pyridoxal, a 3-acylated analogue of pyridoxal-4,5-aminal, a pyridoxine phosphate analogue, and a mixture thereof.

27. The method according to claim 24 wherein the vitamin B6 related compound is pyridoxal-5-phosphate.

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28. The method according to claim 27 wherein the 3-acylated analogue of pyridoxal is:



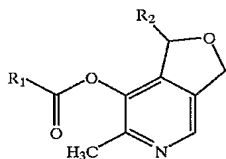
wherein,

R<sub>1</sub> is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

R<sub>1</sub> is dialkylcarbamoxyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxycarbonyl; dialkylcarbamoxyloxy; or

R<sub>1</sub> is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

29. The method according to claim 28 wherein the 3-acylated analogue of pyridoxal-4,5-aminal is



wherein,

R<sub>1</sub> is alkyl, alkenyl, in which alkyl can interrupted by nitrogen, oxygen, or sulfur, and can be unsubstituted or substituted at the terminal carbon with hydroxy, alkoxy, alkanoyloxy, alkoxyalkanoyl, alkoxycarbonyl, or

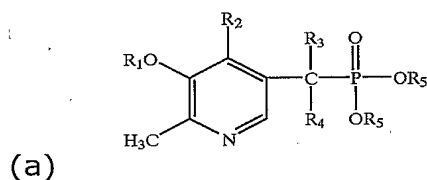
- 54 -

R<sub>1</sub> is dialkylcarbamoyloxy; alkoxy; dialkylamino; alkanoyloxy; alkanoyloxyaryl; alkoxyalkanoyl; alkoxyacetyl; dialkylcarbamoyloxy; or

R<sub>1</sub> is aryl, aryloxy, arylthio, or aralkyl, in which aryl can be substituted by alkyl, alkoxy, amino, hydroxy, halo, nitro, or alkanoyloxy;

R<sub>2</sub> is a secondary amino group.

30. The method according to claim 28 wherein the pyridoxine phosphate analogue is selected from a group consisting:



wherein,

R<sub>1</sub> is hydrogen or alkyl;

R<sub>2</sub> is -CHO-, -CH<sub>2</sub>OH, -CH<sub>3</sub>, -CO<sub>2</sub>R<sub>6</sub> in which R<sub>6</sub> is hydrogen, alkyl, aryl; or

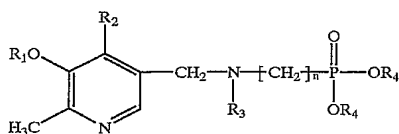
R<sub>2</sub> is -CH<sub>2</sub>-O alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of R<sub>1</sub>;

R<sub>3</sub> is hydrogen and R<sub>4</sub> is hydroxy, halo, alkoxy, alkanoyloxy, alkylamino, or arylamino; or

R<sub>3</sub> and R<sub>4</sub> are halo; and

R<sub>5</sub> is hydrogen, alkyl, aryl, aralkyl, or -CO<sub>2</sub>R<sub>7</sub> in which R<sub>7</sub> is hydrogen, alkyl, aryl, or aralkyl;

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(b)

wherein,

$R_1$  is hydrogen or alkyl;

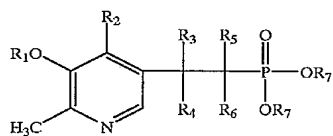
$R_2$  is  $-\text{CHO}$ ,  $-\text{CH}_2\text{OH}$ ,  $-\text{CH}_3$ ,  $-\text{CO}_2\text{R}_5$  in which  $R_5$  is hydrogen, alkyl, aryl; or

$R_2$  is  $-\text{CH}_2\text{-O}$  alkyl in which alkyl is covalently bonded to the oxygen at the 3-position instead of  $R_1$ ;

$R_3$  is hydrogen, alkyl, aryl, aralkyl,

$R_4$  is hydrogen, alkyl, aryl, aralkyl, or  $-\text{CO}_2\text{R}_6$  in which  $R_6$  is hydrogen, alkyl, aryl or aralkyl;

$n$  is 1 to 6; and



(c)

wherein,

$R_1$  is hydrogen or alkyl;

$R_2$  is  $-\text{CHO}$ -,  $\text{CH}_2\text{OH}$ -,  $-\text{CH}_3$ ,  $-\text{CO}_2\text{R}_8$  in which  $R_8$  is hydrogen, alkyl, aryl; or

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R<sub>2</sub> is -CH<sub>2</sub>-O alkyl- in which alkyl is covalently bonded to the oxygen at the 3-position instead of R<sub>1</sub>;

R<sub>3</sub> is hydrogen and R<sub>4</sub> is hydroxy, halo, alkoxy, or alkanoyloxy; or

R<sub>3</sub> and R<sub>4</sub> can be taken together to form =O;

R<sub>5</sub> and R<sub>6</sub> are hydrogen; or

R<sub>5</sub> and R<sub>6</sub> are halo;

R<sub>7</sub> is hydrogen, alkyl, aryl, aralkyl, or -CO<sub>2</sub>R<sub>8</sub> in which R<sub>8</sub> is hydrogen, alkyl, aryl, or aralkyl.

31. The method according to any one of claims 24 to 30, wherein the patient is susceptible to hepatotoxicity.

32. The method according to any one of claims 24 to 31 wherein the cardiovascular disease is selected from a group consisting: congestive heart failure, myocardial ischemia, arrhythmia, myocardial infarction, ischemic stroke, hemorrhagic stroke, coronary artery disease, hypertension (high blood pressure), atherosclerosis (clogging of the arteries), aneurysm, peripheral artery disease (PAD), thrombophlebitis (vein inflammation), diseases of the heart lining, diseases of the heart muscle, carditis, congestive heart failure, endocarditis, ischemic heart disease, valvular heart disease (malfunction of a valve or valves in the blood vessels of the heart), arteriosclerosis (hardening of the arteries), acute coronary syndrome (ACS), deep vein thrombosis (DVT), Kawazaki disease, high cholesterol, restinosis, late vein graft failure and heart transplant.

33. The method according to any one of claims 24 to 32 wherein the dose of the HMG CoA reductase inhibitor is between 0.1 and 1000 mg per day.

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34. The method according to any one of claims 24 to 32 wherein the dose of the HMG CoA reductase inhibitor is 10 mg per day.

35. The method according to any one of claims 24 to 32 wherein the dose of the HMG CoA reductase inhibitor is 20 mg per day.

36. The method according to any one of claims 24 to 32 wherein the dose of the vitamin B6 related compound is between 0.1 to 50 mg/kg per day.

37. The method according to any one of claims 24 to 32 wherein the dose of vitamin B6 related compound is between 1 to 15 mg/kg per day.